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Remarks

The Office Action mailed July 21, 2006 has been received and reviewed. Claims 18 and 19 having been added, the pending claims are claims 1-9 and 13-19. Support for new claims 18 and 19 is found throughout the specification. For example, support for new claims 18 and 19 is found in Example 3, page 19, lines 4-14 of U.S. Provisional Application Serial No. 60/418,822, filed October 15, 2002, to which the instant application claims priority, and which is incorporated by reference into the instant application (see page 1, lines 8-10 of the instant application). Reconsideration and withdrawal of the rejections are respectfully requested.

Examiner Interview

An interview was held between Patent Examiner Zachariah Lucas, Supervisory Patent Examiner Bruce Campell, and Applicants' Representative, Nancy Johnson, at the U.S. Patent and Trademark Office in Alexandria, Virginia, on January 24, 2006, in which the rejections under 35 U.S.C. §102(e) and 35 U.S.C. §103(a) were discussed. Examiners Lucas and Campell are thanked for the courtesy of this interview.

The 35 U.S.C. §102 Rejection

The Examiner rejected claims 1-6 and 16 under 35 U.S.C. §102(e) as being anticipated by Madonna et al. (U.S. 2004/0224359). This rejection is traversed.

Provisional Application 60/418,822 provides support for the method of claims 1-6 and 16

The Examiner asserted that Provisional Application 60/418,822 "fails to provide adequate descriptive support for the present claims . . . In particular, there is no disclosure in the provisional application of embodiments wherein free (i.e. not immobilized onto a substrate) parent phage is present in the sample at the time the progeny phage are released from the parent infected cells in the sample" (page 3, Office Action mailed July 21, 2006). Applicants respectfully submit that "[t]here is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed (*Wertheim*, 541 F.2d at 262, 191

USPQ at 96) and, generally, there is an inverse correlation between the level of skill and knowledge in the art and the specificity of disclosure necessary to satisfy the written description requirement. Information which is well known in the art need not be described in detail in the specification. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986)(M.P.E.P. § 2163).

Applicants respectfully submit that the replication of phage in a host bacteria cell and the lysis of the bacterial cell to release new phage are well understood processes of the life cycle of a virus. Applicants submit that it would, thus, be well known to one of skill in the art that phage lysis and release of new phage particles could occur at any of many points in the method disclosed by Example 3 of Provisional Application 60/418,822. Applicants submit that claims 1-6 and 16 have support in Provisional Application 60/418,822. Reconsideration and withdrawal of the rejection of claims 1-6 and 16 under 35 U.S.C. §102(e) is requested.

Madonna et al. does not teach and every element of the method of claims 1-6 and 16

The Examiner asserted that "there is no disclosure in the provisional application of embodiments wherein free (i.e. not immobilized onto a substrate) parent phage is present in the sample at the time the progeny phage are released from the parent infected cells in the sample. Therefore the present claims do not have the benefit of priority to the earlier provisional application" (page 3, Office Action mailed July 21, 2006). While Applicants disagree, Applicants submit that such a teaching cannot be found in Madonna et al. Applicants submit that the same analysis that has been applied in the determination of priority to U.S. Provisional Application Serial No. 60/418,822 must also be applied to Madonna et al., for a determination of anticipation. Applicants submit that such an analysis indicates that Madonna et al. does not teach each and every element of the claimed invention and, thus, does not anticipate the method of claims 1-16 and 16. Specifically, Applicants submit that Madonna et al. does not teach a method comprising:

> contacting the sample with bacteriophage comprising a binding agent . . . ;

incubating the sample under conditions effective for the bacteriophage comprising a binding agent to infect the bacterial cell, and if a bacterial cell is present in the sample and has been infected by the bacteriophage comprising a binding agent, form new bacteriophage and release new bacteriophage into the sample, wherein the new bacteriophage do not comprise a binding agent;

contacting the sample with a substrate comprising immobilized ligand for the binding agent . . . ;

removing the complexes of bacteriophage . . . ; and

detecting new bacteriophage in the sample" (claim 1).

Applicants submit that, at best, Madonna et al. teaches "*[e]ventually* the infected target bacterium lyses and the replicated bacteriophages are released into the liquid solution" (page 2, column 1, lines 6-8 (emphasis added)). Thus, Madonna et al. does not teach each and every element of the method of claims 1-6 and 16. Reconsideration and withdrawal of this rejection of claims 1-6 and 16 as anticipated by Madonna et al. (U.S. 2004/0224359) is respectfully requested.

Rejection of Claim 16

In rejecting claim 16, the Examiner asserted that "because the claim is silent as to when the progeny phage are released from the parent phage infected cells relative to the time at which the parent phage are removed from the sample, the claim is considered generic to claim 1. The rejection is therefore extended to this claim for the same reasons as described with respect to claim 1 . . . i.e., because the priority application fails to provide sufficient descriptive support for claim 1, it also fails to provide adequate support for the full scope of claim 16" (page 4, Office Action mailed July 21, 2006). Applicants do not understand the Examiner's reasoning. The Examiner has asserted that U.S. Provisional Application Serial No. 60/418,822 does not provide support for the species exemplified in claim 1. From this the Examiner reasons that, because there is not support for the one species exemplified in claim 1, there is not support for the genus. Applicants respectfully submit that the Examiner is reasoning is incorrect. Applicants submit that Example 3 (page 18-19) of U.S. Provisional Application Serial No. 60/418,822 provide support for claim 16. Applicants submit that Madonna et al. is, thus, not an anticipatory reference under 35 U.S.C. §102(e) for claim 16. Reconsideration and withdrawal of this rejection of claim 16 under 35 U.S.C. §102(e) is respectfully requested.

The 35 U.S.C. §103 Rejections

Rejection over Madonna et al. further in view of Terlesky, Stroobant, and Petersen

The Examiner rejected claims 6 and 9 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al. as applied to claims 1-6 and 16 and further in view of the teachings of Terlesky et al. (U.S. 2004/0152085), Stroobant et al. (U.S. 2002/0090637), and Petersen et al. (U.S. 2002/00042125). This rejection is respectfully traversed.

Applicants continue to submit that Madonna et al. (U.S. 2004/0224359) does not qualify as prior art under 35 U.S.C. §102(e) and cannot be used in a rejection under 35 U.S.C. §103(a). Applicants further submit that Madonna et al. does not teach the method of claims 1-6 and that the teachings of Terlesky et al., Stroobant et al., or Petersen et al. do not correct this deficiency in the teachings of Madonna et al. Thus, Madonna et al. as applied to claims 1-6 and 16 and further in view of the teachings of Terlesky et al., Stroobant et al., and Petersen et al. does not "render claims 6 and 9 obvious," as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 6 and 9 under 35 U.S.C. §103(a) is requested.

One of the critical, basic elements necessary to establish a *prima facie* case of nonobviousness of the claimed invention is that "there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings" ((MPEP § 2143). Applicants submit that this requisite motivation to combine the teachings of Madonna et al. with any of Terlesky et al., Stroobant et al., or Petersen et al. is absent. Madonna et al teaches methods for detecting low concentrations of bacteria in a liquid solution (see abstract). Terlesky et al. teaches "a substrate for collecting nucleic acids . . . comprising a surface; an aerogel coated on said surface; an active silane attached to said aerogel; and a nucleic acid binding agent attached to said silane" (see abstract). Stroobant et al. teaches "methods for identifying, isolating and comparing proteins and other biomolecules differing between two complex biological samples using affinity chromatography and phage display techniques" (see abstract). Petersen et al. teaches "a cartridge for performing various operations on a fluid sample as the fluid flows through a series of interconnected, interactive regions within the cartridge" (see page 3, paragraph [0042]). Applicants submit that one of ordinary skill in the art would not be motivated to combine the teachings of Madonna et al. with the teachings of Terlesky et al., Stroobant et al., or Petersen et al. to obtain the present invention. Reconsideration and withdrawal of this rejection of claims 6 and 9 under 35 U.S.C. §103(a) is requested.

The Examiner asserted that

> "the teachings of . . . [Terlesky et al., Stroobant et al., or Petersen et al.] are not relied upon to demonstrate that those in the art would have been motivated to use the methods disclosed . . . for the detection of the phage as described in the Madonna reference. Rather, these references are cited only to demonstrate that the alternative substrates identified in these references were known in the art as useful substrates in biological detection assays. See e.g. MPEP 2144.06. Thus, the teachings of these references demonstrate that these substrates are functional equivalents for each other, and it would therefore be prima facie obvious to substitute any of these substrates with those disclosed by Madonna et al. See page 5, Office Action mailed July 21, 2006.

Applicants disagree and submit that the Examiner is applying an incorrect standard for the establishment of functional equivalents. According to MPEP 2144.06, "[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958)." Applicants submit that the Examiner has not established that the functional equivalence is recognized in the prior art; rather the Examiner is merely asserting a personal opinion as to the functional equivalence of the various substrates. Reconsideration and withdrawal of this rejection of claims 6 and 9 under 35 U.S.C. §103(a) is requested.

Rejection over Madonna et al. further in view of Teodorescue et al.

The Examiner rejected claims 7 and 8 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al., as applied to claims 1-6, and further in view of Teodorescue et al. (U.S. Patent No. 4,797,363). This rejection is respectfully traversed.

Applicants continue to submit that Madonna et al. (U.S. 2004/0224359) does not qualify as prior art under 35 U.S.C. §102(e) and cannot be used in a rejection under 35 U.S.C. §103(a). Applicants submit that Madonna et al. does not teach a method that is the same as the method of claims 1-6. Further, Applicants submit that the teachings of Teodorescue et al. do not correct this deficiency in the teachings of Madonna et al. Thus, Madonna et al., as applied to claims 1-6 and further in view of the teachings of Teodorescue et al., does not render claims 7 and 8 obvious, as asserted by the Examiner. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Further, Applicants submit that this requisite motivation to combine the teachings of Madonna et al. with Teodorescue et al. is absent. Madonna et al. teach methods for detecting low concentrations of bacteria in a liquid solution, wherein a low concentration of bacteriophage are used to infect the bacteria (see abstract). Teodorescue et al. teach methods "for the identification and quantification of molecular and cellular materials . . . wherein bacteriophage are used, in a manner similar to antibodies, as "visualizers" to bind to the molecular or cellular materials (see abstract; col. 2, lines 58-68; and col. 3, lines 43-45). Applicants submit that one of ordinary skill in the art would not be motivated to combine the very different methods taught by Madonna et al. and Teodorescue et al. to obtain the present invention. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

The Examiner asserted that

> "[w]hile there may be insufficient motivation to combine the methods of these references in general, those of ordinary skill would nonetheless recognize that the teachings of Teodorescue . . . would be equally applicable to other situations were phage detection is desired, i.e. from the teachings of Teodorescue, those of ordinary skill in the art would have been made aware of an alternative technique for the detection of phage from that disclosed by Madonna. See e.g, MPEP 2144.06. Because those in the art would have recognized that this alternative

> technique of phage detection is a functional equivalent of the methods for phage detection provided by Madonna, there is sufficient basis to establish a prima facie case of obviousness. . . See page 6, Office Action mailed July 21, 2006.

Applicants disagree and again submit that the Examiner is applying an incorrect standard for the establishment of functional equivalents. According to MPEP 2144.06, "[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958)." Applicants submit that the Examiner has not established that the functional equivalence is recognized in the prior art; rather the Examiner is merely asserting a personal opinion as to the functional equivalence of the various substrates. Reconsideration and withdrawal of this rejection of claims 7 and 8 under 35 U.S.C. §103(a) is requested.

Rejection over Madonna et al. further in view of Olsvik et al. and Yazdankhah et al.

The Examiner rejected claims 13-15 and 17 under 35 U.S.C. §103(a) as being unpatentable over Madonna et al. as applied to claims 1-6 and 16 above, and further in view of the teachings of Olsvik et al. (Clin Micro. Rev., 7:43-54) and Yazdankhah et al. (Vet. Micro., 62:17-26). This rejection is respectfully traversed.

Applicants continue to submit that Madonna et al. (U.S. 2004/0224359) does not qualify as prior art under 35 U.S.C. §102(e) and cannot be used in a rejection under 35 U.S.C. §103(a).

Claims 13-15 and 17 are drawn to a method comprising:

"*incubating* the sample under conditions effective for the bacteriophage comprising a binding agent to infect the bacterial cell . . . ;

contacting the sample with a first substrate comprising immobilized ligand for the binding agent . . . ;

removing the complexes of bacteriophage comprising a binding agent and first substrate comprising immobilized ligand from the sample;

contacting the sample with a second substrate comprising immobilized binding agent specific for the new bacteriophage . . . ;

removing the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage; and

detecting the complexes of new bacteriophage and second substrate comprising immobilized binding agent for the new bacteriophage."

Applicants submit that the combined teachings of Madonna et al. with Olsvik et al. and Yazdankhah et al. do not teach a method with all of the steps of claims 13-15 and 17, as outlined above.

Further, Applicants submit that the requisite motivation to combine the teachings of Madonna et al. with Olsvik et al. and Yazdankhah et al. is absent. Madonna et al. teach methods for detecting low concentrations of bacteria in a liquid solution, wherein immunomagnetic separation is used to separate target bacterium from other constituents in the mixture, wherein a low concentration of a bacteriophage for the target bacterium is subsequently used to infect target bacteria, and wherein Matrix assisted laser desorption ionization/time-of-flight-mass spectroscopy (MALDI/TOF-MS) is used to determine if proteins associated with a bacteriophage are present (see abstract).

Yazdankhah et al. teach a method of detecting *Staphylococcus* bacteria in milk samples by the use of magnetic beads coated with monoclonal antibodies specific to the *Staphylococcus* bacteria. Applicants submit that the teachings of Yazdankhah et al. are limited solely to the detection of bacteria, and are completely silent as to the detection of bacteriophage. Applicants submit that one of ordinary skill in the art would not be motivated to combine the disparate teachings of Madonna et al. with Yazdankhah et al. to obtain the method of claims 13-15 and 17.

As Applicants have previously presented (see page 8 of the Amendment and Response filed March 16, 2005), Olsvik et al. is a review of magnetic separation techniques for use in diagnostic microbiology. The very limited teachings of Olsvik et al. relating to the detection of bacteriophage (referred to therein as "viruses") are limited to the use of oligonucleotide probes linked to magnetic beads to be used as primers in a polymerase chain reaction (PCR) for the direct *detection of viral RNA or DNA in a sample* (see Olsvik et al. pages 50-51 (emphasis added)) and the use of "coated magnetic beads . . . to extract HIV *antigen* from serum and blood . . . [that b]oth *antigen* and *infected cells* attached to the beads could be identified" (see page 51, column 1, paragraph 2 of Olsvik et al. (emphasis added)), Applicants submit that Olsvik does not teach forming a complex between the new bacteriophage and the second substrate comprising immobilized binding agent for the new bacteriophage. Applicants submit that one of ordinary skill in the art would not be motivated to combine the disparate teachings of Madonna et al. with Olsvik et al. to obtain the method of claims 13-15 and 17.

The Examiner asserted that Olsvik teaches

> that immunomagnetic separation was known in the art 'to be suitable for detection of prokaryotic organisms such as bacteria and **viruses**. Thus, the reference clearly indicates that those in the art would have been aware that this technique would be useful both for the detection of bacteria as is described in the reference, and in methods for the detection of viruses. Thus, the reference indicates that the use of detection techniques using immunomagnetic separation described by the cited references would have been recognized as a functional equivalent for the mass spectroscopy methods disclosed by Madonna. See page 7-8 of Office Action mailed July 21, 2006 (emphasis in original).

Applicants adamantly, yet respectfully disagree. Applicants submit that the Examiner's interpretation of "functional equivalents" is again flawed. As previously discussed, MPEP 2144.06 states that "[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958)." Applicants submit that the Examiner has not established that the functional equivalence is recognized in the prior art; rather the Examiner is merely asserting a personal opinion as to the functional equivalence of the various substrates. Reconsideration and withdrawal of this rejection of claims 13-15 and 17 under 35 U.S.C. §103(a) is requested.

The Examiner asserted "[b]ecause claim 17 is generic to claim 13, and as the priority application lacks adequate support for claim 13, and therefore the full scope of claim 17, this claim is also rejected for the same reason as described with respect to claim 13" (page 8 of Office Action mailed July 21, 2006). Applicants disagree. As previously discussed above in the section addressing the rejection of claim 16 under 35 U.S.C. §102(e), Applicants respectfully submit that the Examiner's reasoning that, because one exemplified species is not supported, the generic claim is necessarily not supported, is in error. Applicants submit that Example 3 (page 18-19) of U.S. Provisional Application Serial No. 60/418,822 provides support for "generic" claim 17. Applicants submit that Madonna et al. does not qualify as prior art under 35 U.S.C. §102(e) for claim 17. Reconsideration and withdrawal of this rejection of claim 17 under 35 U.S.C. §103(a) is requested.

In view of the above discussion, reconsideration and withdrawal of this rejection of claims 13-15 and 17 under 35 U.S.C. §103(a) is requested.

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Summary

It is respectfully submitted that the pending claims 1-9 and 13-19 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted
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NAJ/skd

CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Commissioner for Patents, Mail Stop Amendment, P.O. Box 1450, Alexandria, VA 22313-1450, on this 20th day of October, 2006, at 2:55pm (Central Time).

By: Sue Dombroske
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